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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MONIKA HEDDING-ECKERICH

Appeal 2009-013138
Application 10/511,026
Technology Center 1600

Decided: February 1, 2010

Before DEMETRA J. MILLS, LORA M. GREEN, and
JEFFREY N. FREDMAN, *Administrative Patent Judges.*

FREDMAN, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to methods of treatment using uridine-5'-monophosphate or cytidine-5'-monophosphate and pharmaceutical compositions. We have jurisdiction under 35 U.S.C. § 6(b). We reverse and enter new grounds of rejection.

Statement of the Case

The claims are directed to methods of treating pathologies of the peripheral nervous system or stimulating nerve regeneration methods involving administering uridine-5'-monophosphate or cytidine-5'-monophosphate, as well as to pharmaceutical compositions including uridine-5'-monophosphate or cytidine-5'-monophosphate. The Specification acknowledges that "[i]n clinical studies on patients with a polyneuropathy the external application of a mixture of cytidine and uridine led to an amelioration of the typical symptoms of polyneuropathy" (Spec. 2, ll. 17-18). The Specification also notes that a "study on Wistar rats proved the good effectiveness of the active agent combination of uridine monophosphate (UMP) and cytidine monophosphate (CMP) with respect to the regeneration of traumatically affected peripheral nerves" (Spec. 2, ll. 20-22).

The Claims

Claims 1-17 are on appeal. Claims 1, 6, and 7 are representative and read as follows:

> 1. A method of using uridine-5'-monophosphate or cytidine-5'-monophosphate for the treatment of affections of the peripheral nervous system and/or for the stimulation of the regeneration of nerves, comprising administering uridine-5'- monophosphate or cytidine-5'-monophosphate to a patient in need thereof.
>
> 6. A method of using uridine 5'-monophosphate or cytidine-5'-monophosphate for the manufacture of a pharmaceutical composition for the treatment of affections of the peripheral nervous system and/or for the stimulation of the regeneration of nerves, comprising adding uridine-5'-

monophosphate or cytidine-5'-monophosphate to a pharmaceutical composition.

7. Pharmaceutical composition consisting of uridine-5'-monophosphate or cytidine-5'-monophosphate as pharmaceutically active ingredient optionally together with physiologically acceptable carriers, adjuvants and/or diluents.

The prior art

The Examiner relies on the following prior art references to show unpatentability:

Connolly et al., *Uridine and its nucleotides : biological actions, therapeutic potentials*, 20 TRENDS PHARMACOLOGICAL SCIENCES 218-225 (1999).

The issue

The Examiner rejected claims 1-17 under 35 U.S.C. § 103(a) as obvious over Connolly (Ans. 3-5).

The Examiner finds that "Connolly teaches that there are many disorders of pyrimidine metabolism and those that involve an alteration in uridine metabolism have neurological and system effects" (Ans. 3-4). The Examiner finds that "Connolly differs from the instantly claimed invention in that Connolly teaches the therapeutic benefits of uridine and its nucleotides broadly; however, Connolly explicitly contemplates the use of 'uridine' for treating diabetic neuropathy" (Ans. 5). The Examiner finds that the "term 'uridine'. . . is interpreted to embrace uridine and its nucleotides. Since this group represents a small number of compounds (uridine, UMP, UDP and UTP), the use of UMP would have been readily envisioned by one of ordinary skill in the art" (Ans. 5).

Appellant argues that "Connolly draws a general and speculative conclusion that UMP may prove therapeutic utility in treating neurodegenerative disorders, but does not teach or suggest how" (App. Br. 7). Appellant argues that the "studies cited in Connolly only show electrophysiological changes in some nerve cells and at best suggest possible roles for nucleotides only as neurotransmitters. Nucleotides were not implicated in tissue regeneration, nor was CMP tested in the diabetic neuropathy study" (App. Br. 7).

In view of these conflicting positions, we frame the obviousness issue before us as follows:

Has Appellant demonstrated that the Examiner erred in finding it obvious to treat affections of the peripheral nervous system and/or stimulate regeneration of nerves by administering uridine-5'-monophosphate or cytidine-5'-monophosphate?

Findings of Fact (FF)

1. Connolly teaches that "uridine (and its nucleotides) has crucial functions that help regulate a variety of biological systems" (Connolly 218, col. 2).

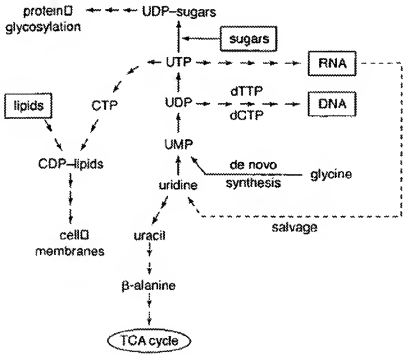
2. Connolly teaches that "uridine and its nucleotides have direct actions on and are capable of modulating peripheral nervous system activity. Uridine, UDP, UTP and UDP-glucose have been shown to depolarize or hyperpolarize amphibian ganglia at submicromolar concentrations" (Connolly 221, col. 1).

3. Connolly teaches that the "observation that chronically administered uridine is able to decrease haloperidol-induced dopamine

release suggests that uridine could be useful in schizophrenia therapy. Clinical results support this hypothesis; uridine shortened the time needed for haloperidol to work and allowed reduction of its maintenance dose" (Connolly 223, col. 2).

4. Connolly teaches that "[c]linically, uridine dramatically promoted recovery from the neural degeneration produced by diabetic neuropathy" (Connolly 224, col. 2).

5. Connolly depicts the metabolism of uridine in Figure 1 as reproduced below:



"Fig. 1. Simple schema showing the metabolism of uridine and some of its derivatives" (Connolly 219, col. 2).

6. The Examiner finds that "Connolly differs from the instantly claimed invention in that Connolly teaches the therapeutic benefits of uridine and its nucleotides broadly" (Ans. 5).

Principles of Law

The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The Supreme Court has emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

"[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR* at 417-18, *quoting In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). The Examiner has the initial burden of establishing a prima facie case obviousness under 35 U.S.C. § 103. *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992) ("[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a prima facie case of unpatentability.").

Analysis

Connolly teaches that "uridine and its nucleotides have direct actions on and are capable of modulating peripheral nervous system activity.

Uridine, UDP, UTP and UDP-glucose have been shown to depolarize or hyperpolarize amphibian ganglia at submicromolar concentrations" (Connolly 221, col. 1; FF 2). Connolly also teaches that "[c]linically, uridine dramatically promoted recovery from the neural degeneration produced by diabetic neuropathy" (Connolly 224, col. 2; FF 4).

However, as the Examiner acknowledges, Connolly never teaches treatment of any particular disease with UMP (FF 6). The Examiner's argument is that since a teaching of uridine and its nucleotides represents a small number of compounds, the use of UMP would have been readily envisioned by the ordinary artisan (*see* Ans. 5). We are not persuaded.

We agree with Appellant that, in view of Connolly, a "person having ordinary skill in the art simply would have had no motivation to try UMP or CMP" (Reply Br. 2). Connolly never mentions the use of UMP as a treatment modality, even in a discussion which mentions uridine, UDP, UTP and UDP-glucose (FF 2).

Conclusion of Law

Appellant has demonstrated that the Examiner erred in finding it obvious to treat affections of the peripheral nervous system and/or stimulate regeneration of nerves by administering uridine-5'-monophosphate or cytidine-5'-monophosphate.

New ground of rejection

Under the provisions of 37 C.F.R. § 41.50(b), we enter the following new grounds of rejection.

Claims 1, 2, 5-9, 12, and 17 are rejected under 35 U.S.C. 102(b) as being unpatentable over Wattig[1].

Claims 6-9 and 17 are rejected under 35 U.S.C. 102(b) as being unpatentable over Tamura[2].

Findings of Fact

7. Wattig teaches that the "effect of nucleotide administration on the regeneration of myelinated nerve fibres following crush injury to the sciatic nerve of the rat was studied" (Wattig 333, abstract).

8. Wattig teaches that a "total of 86 female Wistar rats, aged 7 weeks, were used. Under ether anaesthesia, the right sciatic nerve was crushed under a dissecting microscope for 2 min" (Wattig 334).

9. Wattig teaches that "[t]hereafter operated rats were given daily i.m. injections of uridine monophosphate (UMP, 3.0 mg/kg body wt), cytidine monophosphate (CMP, 2.5 mg/kg body wt), or UMP plus CMP (3.0 and 2.5 mg/kg body wt" (Wattig 334).

10. Wattig teaches that "fibre size in the common peroneal nerve, expressed either as area or diameter, increases significantly between 40 and 60 days with combined UMP/CMP administration. Closely similar changes

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[1] Wattig et. al., *Acceleration of nerve and muscle regeneration by administration of nucleotides – Electroneurophysiological and morphometrical investigations*, 42 ACTA HISTOCHEMICA SUPPL. 333-339 (1992).
[2] Tamura, US 3,852,433, issued Dec. 3, 1974.

affect both myelin area (myelin thickness) and, at a later stage, axon area in UMP/CMP treated rats" (Wattig 337).

11. Tamura teaches "a pharmaceutical composition . . . comprising uridine-5'-monophosphate or its pharmaceutically acceptable salt as active ingredient and a pharmaceutical carrier" (Tamura, col. 1, ll. 51-55).

12. Tamura teaches that the carrier "can be either solid pharmaceutical carrier or diluent when intended for oral administration or as a suppository, or sterile injectable liquid pharmaceutical carrier or diluent when intended for parenteral administration, or liquid pharmaceutical carrier or diluent possibly in admixture with sweetening and/or flavoring agent when intended for oral administration" (Tamura, col. 1, ll. 59-66).

13. Tamura teaches that "200 mg of sodium salt of UMP, pyrogen-free, was dissolved in 2 ml of distilled water for injection, filled into an ampoule, and sterilized" (Tamura, col. 3, ll. 49-51).

14. Tamura teaches "wherein each dosage unit contains from 50 mg to 500 mg of uridine-5'-monophosphate as its sodium salt" (Tamura, col. 4, ll. 38-40).

Principles of Law

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Analysis of whether a claim is patentable over the prior art under 35 U.S.C. § 102 begins with a determination of the scope of the claim. We determine the scope of the claims in patent applications not solely on the basis of the claim language, but upon giving claims their

broadest reasonable construction in light of the specification as it would be interpreted by one of ordinary skill in the art. *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364 (Fed. Cir. 2004). The properly interpreted claim must then be compared with the prior art.

Analysis

Anticipation over Wattig

We begin with claim interpretation. Claim 1 teaches "comprising administering uridine-5'-monophosphate or cytidine-5'-monophosphate to a patient in need thereof". The transitional term "comprising" is "inclusive or open-ended and does not exclude additional, unrecited elements or method steps." *Georgia-Pacific Corp. v. United States Gypsum Co.*, 195 F.3d 1322, 1327, (Fed. Cir. 1999). Therefore, applying the broadest reasonable interpretation to Appellant's use of the term "comprising" in claim 1 results in a claim which can encompass the administration of both uridine-5'-monophosphate and cytidine-5'-monophosphate.

Wattig teaches a method of using UMP and CMP for the stimulation of the regeneration of nerves in a crush injury model, comprising administering UMP and CMP to the wistar rats suffering the crush injury (FF 7-9). Wattig teaches that the administration of UMP and CMP successfully stimulated regeneration of nerves (FF 10).

With regard to claim 2[3], Wattig teaches the use of uridine-5'-monophosphate (FF 8-9).

With regard to claims 5 and 12, Wattig teaches administration of a dose of up to 5.5 mg/kg body weight of UMP and CMP which reasonably

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[3] We note that uridine is misspelled as "uridin" in claim 2.

satisfies the requirement for a minimum daily dose of between 1 and 100 mg (FF 9).

With regard to claim 6, Wattig teaches preparing UMP and CMP for intramuscular injection (FF 9).

With regard to claims 7-8, Wattig teaches pharmaceutical compositions which consist of UMP or CMP with a pharmaceutically acceptable carrier, in concentrations of 3.0 mg/kg body weight (FF 8-9).

With regard to claims 9 and 17, Wattig teaches that the pharmaceutical compositions are suitable for intramuscular injection (FF 9).

Anticipation over Tamura

We begin with claim interpretation. Claim 6 has a preamble in which the manufacture is performed "for the treatment of affections of the peripheral nervous system and/or for the stimulation of the regeneration of nerves". However, a preamble is not limiting "where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention." *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed.Cir.2002). In the instant case, Claim 6 defines a complete invention in the claim body, where the manufacture comprises "adding uridine-5'-monophosphate or cytidine-5'-monophosphate to a pharmaceutical composition". Therefore, the preamble of claim 6 is not found to limit the claim.

Tamura teaches a method satisfying Claim 6 in which "200 mg of sodium salt of UMP, pyrogen-free, was dissolved in 2 ml of distilled water

for injection, filled into an ampoule, and sterilized" (Tamura, col. 3, ll. 49-51; FF 13).

With regard to claim 7, Tamura teaches "a pharmaceutical composition . . . comprising uridine-5'-monophosphate or its pharmaceutically acceptable salt as active ingredient and a pharmaceutical carrier" (Tamura, col. 1, ll. 51-55; FF 11).

With regard to claim 8, Tamura teaches "wherein each dosage unit contains from 50 mg to 500 mg of uridine-5'-monophosphate as its sodium salt" (Tamura, col. 4, ll. 38-40; FF 14).

With regard to claims 9 and 17, Tamura teaches that "200 mg of sodium salt of UMP, pyrogen-free, was dissolved in 2 ml of distilled water for injection, filled into an ampoule, and sterilized" (Tamura, col. 3, ll. 49-51; FF 13).

SUMMARY

In summary, we reverse the rejection of claims 1-17 under 35 U.S.C. § 103(a) as obvious over Connolly.

This decision also contains new grounds of rejection pursuant to 37 C.F.R. § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 C.F.R. § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

Claims 1, 2, 5-9, 12, and 17 are subject to the new grounds of rejection. Claims 3, 4, 10, 11, and 13-16 are not subject to these new grounds of rejection.

37 C.F.R. § 41.50(b) also provides that the Appellants, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

(1) Reopen prosecution. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the Examiner, in which event the proceeding will be remanded to the Examiner. . . .

(2) Request rehearing. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

REVERSED, § 41.50(b)

dm

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